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Abstract

The cholinergic efferent network from the medial septal nucleus to the hippocampus has an important role in learning and memory processes (Mesulam, et. al. *Neuroscience* 1983). This cholinergic projection can generate theta oscillations in the hippocampus to efficiently encode novel information (Dupret, et al. *Neuron* 2013). Hippocampal cholinergic neurostimulating peptide (HCNP) induces acetylcholine synthesis in medial septal nuclei (Ojika, et al. *Brain Res.* 1992). HCNP is processed from the N-terminal region of a 186 amino acid, 21 kD HCNP precursor protein called HCNP-pp (Ojika K, et al. *Prog. Neurobiol.* 2000) [also known as Raf kinase inhibitory protein (RKIP) and phosphatidylethanolamine-binding protein 1 (PEBP1)]. In this study, we generated HCNP-pp knockout (KO) mice and assessed their cholinergic septo-hippocampal projection, local field potentials in CA1, and behavioural phenotypes. No significant behavioural phenotype was observed in HCNP-pp KO mice. However, theta power in the CA1 of HCNP-pp KO mice was significantly reduced because of fewer cholineacetyltransferase-positive axons in the CA1 stratum oriens. These observations indicated disruption of cholinergic activity in the septo-hippocampal network. Our study demonstrates that HCNP may be a cholinergic regulator in the septo-hippocampal network.